

What is claimed is:

1. A process for the preparation of the  $\alpha$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide  
5 comprising:

- f) carrying out the addition reaction of methanesulfonic acid and 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-  
10 [(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide in a solvent selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> aliphatic alcohols or the mixtures thereof, optionally with the addition of the other C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol;  
15 g) adding, if necessary, a solvent selected from the group consisting of the esters of lower carboxylic acids and C<sub>1</sub>-C<sub>4</sub> aliphatic alcohols;  
20 h) optionally inoculating the reaction mixture with the  $\alpha$ -crystal form;  
i) stirring the reaction mixture for the time necessary for crystallization of the  $\alpha$ -crystal form;  
25 j) isolating the  $\alpha$ -crystal form from the reaction mixture.

2. A process according to claim 1 in which the addition reaction is carried out using not more than

0.99 equivalent, especially from 0.95 to 0.99 equivalents of methanesulfonic acid per 1 equivalent of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide.

- 5           3. A process according to Claims 1-2, in which the addition reaction is carried out in an alcohol selected from the group comprising *n*-propyl alcohol, isopropyl alcohol, *n*-butyl alcohol, *tert*-butyl alcohol and the mixtures thereof with ethyl alcohol.
- 10           4. The method according to Claims 1-3 in which the addition reaction is carried out in the mixture containing from 0 to 50% of ethyl alcohol and from 50 to 100% of *n*-propyl alcohol (v/v).
5. The method according to Claims 1-3 in which the  
15 addition reaction is carried out in the mixture containing from 0 to 50% of ethyl alcohol and from 50 to 100% of isopropyl alcohol (v/v).
6. The method according to Claims 1-3 in which the  
20 addition reaction is carried out in the mixture containing from 0 to 50% of ethyl alcohol and from 50 to 100% of *n*-butyl alcohol.
7. The method according to Claims 1-3 in which the  
25 addition reaction is carried out in the mixture containing from 0 to 50% of ethyl alcohol and from 50 to 100% of *tert*-butyl alcohol.
8. A process according to claim 1 in which the addition reaction is carried out using 1 equivalent of

methanesulfonic acid per 1 equivalent of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide.

9. A process according to Claim 8 comprising:

- 5 a) the addition reaction of methanesulfonic acid and 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a solvent selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> aliphatic alcohols, optionally with the addition of the other C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol;
- 10 b) adding a solvent selected from the group consisting of the esters of lower carboxylic acids and C<sub>1</sub>-C<sub>4</sub> aliphatic alcohols;
- 15 c) inoculating the reaction mixture with the  $\alpha$ -crystal form;
- d) stirring the reaction mixture for the time necessary for crystallization of the  $\alpha$ -crystal form;
- 20 e) isolating the  $\alpha$ -crystal form from the reaction mixture.

10. A process according to Claims 1-9 in which the addition reaction is carried out with stirring while maintaining internal temperature of the mixture within the range from room temperature to boiling temperature of the reaction mixture.

25

11. A process according to Claims 1-10 in which the  $\alpha$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide thus obtained is essentially free of the  $\beta$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide or any other crystalline solids.

12. A process according to Claims 1-11 in which the  $\alpha$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide thus obtained shows on X-ray powder diffraction diagram peaks at  $2\theta$  angles of approximately: 4.9; 18.6; 19.1; 23.2 and 28.6°, obtained for radiation of CuK $\alpha$  and the wavelength  $\lambda=1,54056 \text{ \AA}$ .

13. The method according to Claims 1-12 in which the  $\alpha$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide thus obtained shows on X-ray powder diffraction diagram the peaks of relative intensity over 20% at  $2\theta$  angles of approx.: 10.5; 14.9; 16.5; 17.7; 18.1; 18.6; 19.1; 21.3; 21.6; 22.7; 23.2; 23.8; 24.9; 27.4; 28.0 and 28.6°.

14. Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide.

15 Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a crystalline form.

16. Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a crystalline Form I which shows on X-ray powder diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å peaks of relative intensity over 20% at  $2\theta$  angles about: 16.94, 19.80, 20.08, 20.51, 21.28, 21.65, 21.98, 22.70 and 23.07°.

16. Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a crystalline Form I according to Claim 15, characteristic in that its X-ray powder diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å is essentially identical with that presented on Fig. 8.

17. Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a crystalline Form II which shows on X-ray powder

diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å peaks of relative intensity over 20% at  $2\theta$  angles about: 17.23, 17.62, 18.72, 19.90, 20.23, 21.25, 21.59, 22.05, 22.44, 23.38, 23.68, 24.48, 25.41, 26.10 and 28.39°.

18. Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in a crystalline Form II according to Claim 17, characteristic in that its X-ray powder diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å is essentially identical with that presented on Fig. 9.

19. A mixture of the crystalline Forms I and II of dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide which shows on X-ray powder diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å peaks of relative intensity over 20% at  $2\theta$  angles about: 16.91, 17.60, 18.69, 19.78, 20.50, 21.60, 22.00, 22.70, 23.07, 24.49, 26.13 and 27.25°.

20. The mixture of the crystal Forms I and II of Dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide according to Claim 19, characteristic in that its X-ray powder

diffraction diagram obtained for radiation of CuK $\alpha$  at the wavelength  $\lambda=1.54056$  Å is essentially identical with that presented on Fig. 10.

21. The use of any of the crystalline form of  
5 dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide selected from the group comprising the Forms I and II and the mixtures thereof, for the preparation of a  
10 pharmaceutical composition having anti-neoplastic activity.

22. The pharmaceutical composition of  
dimethanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-  
15 3-yl)pyrimidin-2-ylamino)phenyl]benzamide selected from the group comprising the crystalline forms I and II and the mixtures thereof, together with the pharmaceutically acceptable carriers and/or excipients.